Case# 10/826472
STN
AS 12/12/02

10826472-121207-stnc.txt

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FILE 'MEDLINE' ENTERED AT 16:24:36 ON 12 DEC 2007

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FILE 'BIOTECHNO' ENTERED AT 16:24:36 ON 12 DEC 2007
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=> s irradiation and inflammation
L1        5392 IRRADIATION AND INFLAMMATION

=> s l1 and brain
L2         236 L1 AND BRAIN

=> s l2 and indomethacin
L3           4 L2 AND INDOMETHACIN

=> s l2 and anti-inflammatory
L4          18 L2 AND ANTI-INFLAMMATORY

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5          11 DUP REM L4 (7 DUPLICATES REMOVED)

=> s l5 and py<2003
   2 FILES SEARCHED...
L6           2 L5 AND PY<2003

=> dup rem l4
PROCESSING COMPLETED FOR L4
L7          11 DUP REM L4 (7 DUPLICATES REMOVED)

=> dup rem l3
PROCESSING COMPLETED FOR L3
L8           3 DUP REM L3 (1 DUPLICATE REMOVED)

=> disp l6 ibib abs 1-2

L6   ANSWER 1 OF 2  SCISEARCH  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    2002:862807  SCISEARCH
THE GENUINE ARTICLE: 602WW
TITLE:               Cyclooxygenase-2 modulates   ***brain***
                       ***inflammation***  -related gene expression in central
                     nervous system radiation injury
AUTHOR:              Kyrkanides S; Moore A H; Olschowka J A; Daeschner J C;
                     Williams J P; Hansen J T; O'Banion M K (Reprint)
CORPORATE SOURCE:    Univ Rochester, Sch Med & Dent, Med Ctr, Dept Neurobiol &
                     Anat, 601 Elmwood Ave, Box 603, Rochester, NY 14642 USA
                     (Reprint); Univ Rochester, Sch Med & Dent, Med Ctr, Dept
                     Neurobiol & Anat, Rochester, NY 14642 USA; Univ Rochester,
                     Sch Med & Dent, Dept Dent, Rochester, NY 14642 USA; Univ
                     Rochester, Sch Med & Dent, Dept Radiat Oncol, Rochester,
                     NY 14642 USA; Univ Rochester, Sch Med & Dent, Dept Neurol,
```

Rochester, NY 14642 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR BRAIN RESEARCH, (***15 AUG 2002***) Vol. 104, No. 2, pp. 159-169.
ISSN: 0169-328X.
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ENTRY DATE: Entered STN: 8 Nov 2002
Last Updated on STN: 8 Nov 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the contribution of cyclooxygenase-2 (COX-2) to peripheral ***inflammation*** is well documented, little is known about its role in ***brain*** ***inflammation*** . For this purpose we studied COX-2 expression in the mouse ***brain*** following ionizing radiation in vivo, as well as in murine glial cell cultures in vitro. The possible role of COX-2 in modulating ***brain*** ***inflammation*** was examined utilizing NS-398, a COX-2 selective inhibitor. Our results indicate that COX-2 is significantly induced in astrocyte and microglial cultures by radiation injury as well as in ***brain*** . Increased levels of prostaglandin E-2 in irradiated ***brain*** were reduced by NS-398. Moreover, NS-398 administration significantly attenuated levels of induction for the majority of inflammatory mediators examined, including TNFalpha, IL-1beta, IL-6, iNOS, ICAM-1, and MMP-9. In contrast, the chemokines MIP-2 and MCP-1 showed enhanced levels of induction following NS-398 administration. These results indicate that COX-2 modulates the inflammatory response in ***brain*** following radiation injury, and suggest the use of COX-2 selective inhibitors for the management of CNS ***inflammation*** . (C) 2002 Elsevier Science B.V. All rights reserved.

ACCESSION NUMBER: 2001:472985 SCISEARCH
THE GENUINE ARTICLE: 438MY
TITLE: Ionizing radiation affects 26s proteasome function and associated molecular responses, even at low doses
AUTHOR: Pajonk F (Reprint); McBride W H
CORPORATE SOURCE: Radiol Univ Clin, Dept Radiat Therapy, Hugstetter Str 55, D-79106 Freiburg, Germany (Reprint); Radiol Univ Clin, Dept Radiat Therapy, D-79106 Freiburg, Germany; Univ Calif Los Angeles, Sch Med, Dept Radiat Oncol, Expt Div, Los Angeles, CA USA
COUNTRY OF AUTHOR: Germany; USA
SOURCE: RADIOTHERAPY AND ONCOLOGY, (***MAY 2001***) Vol. 59, No. 2, pp. 203-212.
ISSN: 0167-8140.
PUBLISHER: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 50
ENTRY DATE: Entered STN: 22 Jun 2001
Last Updated on STN: 22 Jun 2001

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background and purpose: Ionizing radiation is known to activate certain signal transduction pathways, the regulation of which could involve post-transcriptional as well as transcriptional mechanisms. One of the most important post-transcriptional pathways in eukaryotic cells is the ATP- and ubiquitin-dependent degradation of proteins by the 26s proteasome. This process controls initiation of many cellular stress

responses, as well as inflammatory responses under control of the transcription factor NF-kappaB. The literature on the relationship between radiation and ***inflammation*** seems somewhat paradoxical. At high doses, radiation is generally pro-inflammatory. On the other hand, low dose radiation has a long history of use in the treatment of inflammatory disease. This suggests the involvement of multiple mechanisms that may operate differentially at different dose levels.

Materials and methods: In this paper, the ability of different doses of ionizing radiation to directly affect 26s proteasome activity was tested in ECV 304 cells. Proteasome activity, I kappaB alpha protein levels, and NF-kappaB activation were monitored.

Results: Inhibition of chymotrypsin-like 20s and 26s proteasome activity was observed immediately after low- and high-dose ***irradiation*** either of cells or purified proteasomes. The inhibitory effect was independent of the availability of the known endogenous proteasome inhibitor heat shock protein 90 (hsp90). Levels of I kappaB alpha, a physiological 26s proteasome substrate, were increased only at low doses (0.25 Gy) and unaltered at higher doses whereas only the highest doses (8 and 20 Gy) activated NF-kappaB.

Conclusions: We conclude that the proteasome is a direct target of ionizing radiation and suggest that inhibition of proteasome function provides a molecular framework within which low dose ***anti*** - ***inflammatory*** effects of radiation, and radiation-induced molecular responses in general, should be considered.

=> disp l8 ibib abs 1-3

L8 ANSWER 1 OF 3 DISSABS COPYRIGHT (C) 2007 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 2004:69095 DISSABS Order Number: AAI3128436
TITLE: Radiation injury and inflammatory inhibition of neurogenesis
AUTHOR: Monje, Michelle Leigh [Ph.D.]; Palmer, Theo D. [advisor]
CORPORATE SOURCE: Stanford University (0212)
SOURCE: Dissertation Abstracts International, (2004) Vol. 65, No. 4B, p. 1716. Order No.: AAI3128436. 104 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 20041217
Last Updated on STN: 20041217

AB In both pediatric and adult patients, cranial radiation therapy causes a debilitating cognitive decline that is poorly understood and currently untreatable. The radiation-induced deficit is characterized by hippocampal dysfunction and previous work has demonstrated a radiation-induced decrease in postnatal hippocampal neurogenesis. This work shows that the deficit in neurogenesis reflects alterations in the microenvironment that regulates progenitor cell fate, as well as a defect in the proliferative capacity of the neural progenitor cell population. Not only is hippocampal neurogenesis ablated, but the remaining neural precursors adopt glial fates and transplants of non-irradiated neural precursor cells fail to differentiate into neurons in the irradiated hippocampus. The inhibition of neurogenesis is accompanied by marked alterations in the neurogenic microenvironment that include disruption of the microvascular angiogenesis associated with adult neurogenesis and a striking increase in the number and activation status of microglia within the neurogenic zone.

Inflammation inhibits neurogenesis and causes dissociation of the neurovascular relationship. Activated microglia have a direct inhibitory effect on neurogenesis, due in part to the elaboration of pro-inflammatory cytokines such as interleukin-6. Inflammatory inhibition

of neurogenesis is due to both a specific block in neuronal differentiation and an overall increase in precursor cell death. The non-steroidal anti-inflammatory drug ***indomethacin*** reduces neuroinflammation and partially restores neurogenesis following ***irradiation*** . Recruited peripheral monocytes/macrophages appear to play a key role. Mice deficient in the chemokine (monocyte chemoattractant protein-1, MCP-1) responsible for monocyte/macrophage recruitment to ***brain*** are completely resistant to the inhibition of neurogenesis that follows ***irradiation*** . These findings provide clear and specific targets for therapeutic intervention.

L8 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2003502774 EMBASE
TITLE: Inflammatory Blockade Restores Adult Hippocampal Neurogenesis.
AUTHOR: Monje M.L.; Toda H.; Palmer T.D.
CORPORATE SOURCE: T.D. Palmer, Stanford University, Department of Neurosurgery, Mail Code 5487, 1201 Welch Road, Stanford, CA 94305-5487, United States. tpalmer@stanford.edu
SOURCE: Science, (6 Dec 2003) Vol. 302, No. 5651, pp. 1760-1765. Refs: 53
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Dec 2003
Last Updated on STN: 30 Dec 2003

AB Cranial radiation therapy causes a progressive decline in cognitive function that is linked to impaired neurogenesis. Chronic ***inflammation*** accompanies radiation injury, suggesting that inflammatory processes may contribute to neural stem cell dysfunction. Here, we show that neuroinflammation alone inhibits neurogenesis and that inflammatory blockade with ***indomethacin*** , a common nonsteroidal anti-inflammatory drug, restores neurogenesis after endotoxin-induced ***inflammation*** and augments neurogenesis after cranial ***irradiation*** .

L8 ANSWER 3 OF 3 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:870545 SCISEARCH
THE GENUINE ARTICLE: 604VY
TITLE: Fructose-1,6-diphosphate attenuates prostaglandin E-2 production and cyclo-oxygenase-2 expression in UVB-irradiated HaCaT keratinocytes
AUTHOR: Ahn S M; Yoon H Y; Lee B G; Park K C; Chung J H; Moon C H; Lee S H (Reprint)
CORPORATE SOURCE: Ajou Univ, Sch Med, Dept Physiol, 56-1 Wonchon Dong, Suwon 442749, South Korea (Reprint); Ajou Univ, Sch Med, Dept Physiol, Suwon 442749, South Korea; Pacific Corp, Skin Res Inst, Skin Res Team, Yongin 449729, South Korea; Seoul Natl Univ, Coll Med, Dept Dermatol, Seoul 110744, South Korea
COUNTRY OF AUTHOR: South Korea
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (OCT 2002) Vol. 137, No. 4, pp. 497-503.
ISSN: 0007-1188.
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST,

LONDON N1 9XW, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44
ENTRY DATE: Entered STN: 15 Nov 2002
Last Updated on STN: 15 Nov 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB 1 Fructose-1,6-diphosphate (FDP), a glycolytic metabolite, is reported to ameliorate ***inflammation*** and inhibit the nitric oxide production in murine macrophages stimulated with endotoxin. It is also reported that FDP has cytoprotective effects against hypoxia or ischaemia/reperfusion injury in ***brain*** and heart. However, underlying mechanisms of its various biological activities are not completely understood.

2 In this study, we examined the effects of FDP on UVB-induced prostaglandin production in HaCaT keratinocytes.

3 Ultraviolet B (UVB, 280-320 nm) ***irradiation*** (30 mJ cm(-2)) increased prostaglandin E-2(PGE(2)) production, which was significantly decreased by FDP in a concentration dependent manner. NS-398, a cyclo-oxygenase-2 (COX-2) selective inhibitor completely inhibited UVB-induced PGE(2) production showing that COX-2 activity is responsible for the increase in PGE(2) production under our experimental conditions.

4 UVB ***irradiation*** increased total COX activity and COX-2 mRNA in HaCaT keratinocytes, which were significantly blocked by FDP in a concentration dependent manner.

5 N-acetylcysteine (NAC) significantly attenuated UVB-induced PGE(2) production, COX activity and COX-2 mRNA expression indicating oxidative components might contribute to these events.

6 FDP reduced UVB-induced increase in cellular reactive oxygen species (ROS) level although it did not show direct radical scavenging effect in the experiment using 1,1-diphenyl-2picrylhydrazil (DPPH). FDP preserved the cellular antioxidant capacity including catalase activity and GSH content after ***irradiation*** .

7 Our data obtained hitherto suggest that FDP may have a protective role in UVB-injured keratinocyte by attenuating PGE(2) production and COX-2 expression, which are possibly through blocking intracellular ROS accumulation.

```
=> s brain tumor and anti inflammatory
L9          122 BRAIN TUMOR AND ANTI INFLAMMATORY

=> s l9 and radiation
L10          14 L9 AND RADIATION

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11           8 DUP REM L10 (6 DUPLICATES REMOVED)

=> s l11 and py<2003
   2 FILES SEARCHED...
L12           4 L11 AND PY<2003

=> disp l12 ibib abs 1-4

L12  ANSWER 1 OF 4      MEDLINE on STN
ACCESSION NUMBER:    96379840      MEDLINE
DOCUMENT NUMBER:     PubMed ID: 8787853
TITLE:               The safety of interstitial chemotherapy with BCNU-loaded
                     polymer followed by ***radiation*** therapy in the
                     treatment of newly diagnosed malignant gliomas: phase I
                     trial.
```

AUTHOR: Brem H; Ewend M G; Piantadosi S; Greenhoot J; Burger P C; Sisti M
CORPORATE SOURCE: Department of Neurosurgery, Johns Hopkins Hospital, Baltimore, MD, USA.
CONTRACT NUMBER: CA-09574 (NCI)
U01-CA52857 (NCI)
SOURCE: Journal of neuro-oncology, ***(1995 Nov)*** Vol. 26, No. 2, pp. 111-23.
Journal code: 8309335. ISSN: 0167-594X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 6 Nov 1996
Last Updated on STN: 6 Nov 1996
Entered Medline: 24 Oct 1996

AB The results of a multi-institutional phase I trial evaluating the safety of surgically implanted biodegradable 1,3-bis(chloro-ethyl)-1-nitrosourea (BCNU) impregnated polymer as the initial therapy for malignant ***brain*** ***tumors*** are reported. This is the first study of locally delivered BCNU and standard external beam . ***radiation*** therapy (XRT) given concurrently. Twenty-two patients were treated at three hospitals. The entry criteria were: single unilateral tumor focus larger than 1 cm3; age over 18 years; Karnofsky Performance Score (KPS) of at least 60 h; and an intra-operative diagnosis of malignant glioma. Twenty-one of twenty-two patients had glioblastoma multiforme. After surgery, seven or eight BCNU-loaded polyanhydride polymer discs (7.7 mg BCNU each) were placed in the resection cavity. Postoperatively, all patients received standard ***radiation*** therapy; none received additional chemotherapy in the first 6 months. Neurotoxicity, systemic toxicity, and survival were assessed. No perioperative mortality was seen. Neurotoxicity was equivalent to that occurring in other series of patients undergoing craniotomy and XRT without local chemotherapy. Systematically, no significant bone marrow suppression occurred, and there were no wound infections. Median survival in this group of older patients (mean age = 60) was 42 weeks, 8 patients survived 1 year, and 4 patients survived more than 18 months. Interstitial chemotherapy with BCNU-polymer with subsequent ***radiation*** therapy appears to be safe as an initial therapy. Several long-term survivors in this group of older patients with predominantly glioblastoma suggests efficacy in some patients. Dose escalation and efficacy trials are planned to further evaluate interstitial chemotherapy for the initial treatment of malignant gliomas.

L12 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 75077351 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1089097
TITLE: Ocular reticulum cell sarcoma.
AUTHOR: Klingele T G; Hogan M J
SOURCE: American journal of ophthalmology, ***(1975 Jan)*** Vol. 79, No. 1, pp. 39-47.
Journal code: 0370500. ISSN: 0002-9394.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197504

ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 10 Mar 1990
Entered Medline: 11 Apr 1975

AB In four of eight cases of reticulum cell sarcoma with ocular involvement diagnosis was made by craniotomy when the signs of a ***brain*** ***tumor*** developed. A fifth case had an isolated intraocular tumor. Of the other three, two were diagnosed by vitreous aspiration and one by cerebrospinal fluid cytology. Ocular reticulum cell sarcoma frequently accompanies or precedes brain involvement. In this form of the disease the ocular lesion is usually a tumor cell infiltrate of the retina. The associated retinochoroiditis leads to marked vitreous clouding and eventual retinal detachment and glaucoma may occur. On the other hand, when intraocular reticulum cell sarcoma occurs in association with the systemic lymph node visceral form of the disease, choroidal involvement is the rule. Vitreous aspiration may confirm the diagnosis at an early stage when clinical and laboratory evaluation reveal no disease outside the globe. The retinal tumor foci are radiosensitive and local ***radiation*** , although not curative, may restore visual acuity. Immunosuppressive therapy given in low doses for ***anti*** - ***inflammatory*** effect may exacerbate the disease.

L12 ANSWER 3 OF 4 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:154551 SCISEARCH
THE GENUINE ARTICLE: QJ112
TITLE: USE OF CORTICOSTEROIDS IN NEUROONCOLOGY
AUTHOR: KOEHLER P J (Reprint)
CORPORATE SOURCE: DE WEVER & GREGORIUS HOSP, DEPT NEUROL, POB 4446, 6401 CX HEERLEN, NETHERLANDS (Reprint)
COUNTRY OF AUTHOR: NETHERLANDS
SOURCE: ANTI-CANCER DRUGS, (***FEB 1995***) Vol. 6, No. 1, pp. 19-33.
ISSN: 0959-4973.
PUBLISHER: RAPID SCIENCE PUBLISHERS, 2-6 BOUNDARY ROW, LONDON, ENGLAND SE1 8NH.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 177
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Glucocorticosteroids (GC) play an important role in the treatment of neuro-oncologic patients. GC are used for the management of malignant ***brain*** ***tumors*** , either primary of secondary, neoplastic epidural spinal cord compression (NESC), as adjuvant chemotherapy of some central nervous system tumors and perioperatively in brain surgery. GC are believed to exert their influence an ***brain*** ***tumors*** mainly by reducing the tumor-associated vasogenic edema, probably by decreasing the increased capillary permeability of the blood-brain barrier (BBB). Experimental as well as clinical studies applying computed tomography, magnetic resonance and PET have supported these theories. However, other mechanisms have been proposed and investigated, such as a reduction of cerebral blood flow and oncolytic effects, the fatter being controversial. The effect of GC is best observed in patients with cerebral metastases and gliomas. Studies on the effect of non-steroidal ***anti*** - ***inflammatory*** drugs (NSAIDs) gave conficting results. Although some prefer methylprednisolone, dexamethasone is the GC given in the majority of neuro-oncologic patients, at an empirically chosen dosage of 4 mg qid. Dose-effect studies in patients with cerebral metastases as well as in patients suffering from NESC have been performed and lower doses in a twice daily regime may be sufficient. Side-effects may be divided in three groups: those originating from the

mineralocorticoid activity, the withdrawal of the drug and the chronic excess GC administration. Steroid myopathy is the most frequent occurring serious side-effect in neuro-oncologic patients. Others include gastrointestinal perforation and hemorrhage, opportunistic infections, steroid diabetes, and skin and facial changes. The most important interaction is that with phenytoin. The influence of dexamethasone on the effects of chemotherapy and radiotherapy is also discussed. New developments in GC treatment include the local administration of dexamethasone.

L12 ANSWER 4 OF 4 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:185275 SCISEARCH
THE GENUINE ARTICLE: FC883
TITLE: GRAVES OPHTHALMOPATHY - ROLE OF MR IMAGING IN ***RADIATION*** -THERAPY
AUTHOR: JUST M (Reprint); KAHALY G; HIGER H P; ROSLER H P; KUTZNER J; BEYER J; THELEN M
CORPORATE SOURCE: UNIV MAINZ KLINIKUM, INST KLIN STRAHLENKUNDE, LANGENBECKSTR 1, W-6500 MAINZ 1, GERMANY (Reprint); UNIV MAINZ KLINIKUM, MED 3 KLIN & POLIKLIN, W-6500 MAINZ 1, GERMANY; DEUTSCH KLIN DIAGNOST, WIESBADEN, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: RADIOLOGY, (***APR 1991***) Vol. 179, No. 1, pp. 187-190.
ISSN: 0033-8419.
PUBLISHER: RADIOLOGICAL SOC NORTH AMER, 20TH AND NORTHAMPTON STS, EASTON, PA 18042.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 19
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Twenty-three patients with Graves ophthalmopathy who underwent ***radiation*** therapy were monitored by means of magnetic resonance (MR) imaging. T2 relaxation times of extraocular muscles and orbital fat, areas of extraocular muscles, and degree of exophthalmos were measured by means of MR imaging at the beginning, at the end, and 3 months after completion of ***radiation*** therapy. As a result, patients with primarily elevated T2 times of extraocular muscles showed a better therapy response regarding muscle thickening than patients with primarily normal T2 times. Elevated T2 times, which probably represent acute inflammatory changes, were markedly decreased at the end of therapy. Therefore, quantitative MR imaging favors the choice of ***anti*** - ***inflammatory*** therapy regimens in patients with elevated T2 times of extraocular muscles. However, the clinical response (activity scores) to the low-dose treatment protocol that was used did not correlate well with primarily elevated T2 times. Furthermore, T2 times increased again after cessation of therapy. Whether a higher ***radiation*** dose or a different fractionation scheme leads to better results must be clarified by means of further study.

=> s radiation and neuroinflammation
L13 25 RADIATION AND NEUROINFLAMMATION

=> s l13 and anti inflammatory
L14 7 L13 AND ANTI INFLAMMATORY

=> dup rem l14
PROCESSING COMPLETED FOR L14

L15 3 DUP REM L14 (4 DUPLICATES REMOVED)

=> disp l15 ibib abs 1-3

L15 ANSWER 1 OF 3 DISSABS COPYRIGHT (C) 2007 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 2004:69095 DISSABS Order Number: AAI3128436
TITLE: ***Radiation*** injury and inflammatory inhibition of neurogenesis
AUTHOR: Monje, Michelle Leigh [Ph.D.]; Palmer, Theo D. [advisor]
CORPORATE SOURCE: Stanford University (0212)
SOURCE: Dissertation Abstracts International, (2004) Vol. 65, No. 4B, p. 1716. Order No.: AAI3128436. 104 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 20041217
Last Updated on STN: 20041217

AB In both pediatric and adult patients, cranial ***radiation*** therapy causes a debilitating cognitive decline that is poorly understood and currently untreatable. The ***radiation*** -induced deficit is characterized by hippocampal dysfunction and previous work has demonstrated a ***radiation*** -induced decrease in postnatal hippocampal neurogenesis. This work shows that the deficit in neurogenesis reflects alterations in the microenvironment that regulates progenitor cell fate, as well as a defect in the proliferative capacity of the neural progenitor cell population. Not only is hippocampal neurogenesis ablated, but the remaining neural precursors adopt glial fates and transplants of non-irradiated neural precursor cells fail to differentiate into neurons in the irradiated hippocampus. The inhibition of neurogenesis is accompanied by marked alterations in the neurogenic microenvironment that include disruption of the microvascular angiogenesis associated with adult neurogenesis and a striking increase in the number and activation status of microglia within the neurogenic zone.

Inflammation inhibits neurogenesis and causes dissociation of the neurovascular relationship. Activated microglia have a direct inhibitory effect on neurogenesis, due in part to the elaboration of pro-inflammatory cytokines such as interleukin-6. Inflammatory inhibition of neurogenesis is due to both a specific block in neuronal differentiation and an overall increase in precursor cell death. The non-steroidal ***anti*** - ***inflammatory*** drug indomethacin reduces ***neuroinflammation*** and partially restores neurogenesis following irradiation. Recruited peripheral monocytes/macrophages appear to play a key role. Mice deficient in the chemokine (monocyte chemoattractant protein-1, MCP-1) responsible for monocyte/macrophage recruitment to brain are completely resistant to the inhibition of neurogenesis that follows irradiation. These findings provide clear and specific targets for therapeutic intervention.

L15 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004032199 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14731075
TITLE: ***Radiation*** -induced edema is dependent on cyclooxygenase 2 activity in mouse brain.
AUTHOR: Moore Amy H; Olschowka John A; Williams Jacqueline P; Paige Sharon L; O'Banion M Kerry
CORPORATE SOURCE: Department of Neurobiology and Anatomy, University of Rochester School of Medicine and Dentistry, 601 Elmwood Avenue, Rochester, New York 14642, USA.
CONTRACT NUMBER: P01 CA11051 (NCI)
R01 NS33553 (NINDS)
SOURCE: Radiation research, (2004 Feb) Vol. 161, No. 2, pp. 153-60. Journal code: 0401245. ISSN: 0033-7587.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 21 Jan 2004
Last Updated on STN: 7 Apr 2004
Entered Medline: 6 Apr 2004

AB Cerebrovascular dysfunction, characterized by compromise of the blood-brain barrier and formation of cerebral edema, is common during the acute period after brain irradiation and may contribute to delayed pathology (e.g. vascular collapse, white matter necrosis) that leads to functional deficits. Another response of normal brain tissue to ***radiation*** is the induction of inflammatory markers, such as cytokine expression and glial activation. In particular, ***radiation*** -induced ***neuroinflammation*** is associated with an elevation in cyclooxygenase 2 (COX2), one of two isoforms of the obligate enzyme in prostanoid synthesis and the principal target of non-steroid ***anti*** - ***inflammatory*** drugs. Since prostanoids serve as autocrine and paracrine mediators in numerous physiological and pathological processes, including vasoregulation, we investigated COX2 protein expression and COX2-mediated prostanoid production in ***radiation*** -induced cerebral edema in male C57/BL6 mice. We found that ***radiation*** induces COX2 protein that is accompanied by specific increases in prostaglandin E(2) and thromboxane A(2) within 4 and 24 h after brain irradiation. Furthermore, we showed that treatment with NS-398, a selective COX2 inhibitor, attenuated prostanoid induction and edema formation. These results suggest that ***radiation*** -induced changes in vascular permeability are dependent on COX2 activity, implicating this enzyme and its products as targets for potential therapeutic treatment/protection from the effects of ***radiation*** on normal brain tissue.

L15 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003577637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14615545
TITLE: Inflammatory blockade restores adult hippocampal neurogenesis.
AUTHOR: Monje Michelle L; Toda Hiroki; Palmer Theo D
CORPORATE SOURCE: Stanford University, Department of Neurosurgery, MSLS P309, Mail Code 5487, 1201 Welch Road, Stanford, CA 94305-5487, USA.
CONTRACT NUMBER: F30 NS04696701 (NINDS)
MH20016-05 (NIMH)
SOURCE: Science (New York, N.Y.), (2003 Dec 5) Vol. 302, No. 5651, pp. 1760-5. Electronic Publication: 2003-11-13.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 30 Dec 2003
Entered Medline: 29 Dec 2003

AB Cranial ***radiation*** therapy causes a progressive decline in cognitive function that is linked to impaired neurogenesis. Chronic inflammation accompanies ***radiation*** injury, suggesting that inflammatory processes may contribute to neural stem cell dysfunction. Here, we show that ***neuroinflammation*** alone inhibits neurogenesis and that inflammatory blockade with indomethacin, a common nonsteroidal

anti - ***inflammatory*** drug, restores neurogenesis after endotoxin-induced inflammation and augments neurogenesis after cranial irradiation.

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FILE LAST UPDATED: 11 Dec 2007 (20071211/ED)

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927009 CAPLUS
DOCUMENT NUMBER: 141:374718
TITLE: Prevention of deficits in neurogenesis with anti-inflammatory agents
INVENTOR(S): ***Monje, Michelle L.*** ; Palmer, Theo D.
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093802	A2	20041104	WO 2004-US11936	20040416
WO 2004093802	A3	20060921		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1622577	A2	20060208	EP 2004-750277	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: US 2003-463769P P 20030417
US 2003-519562P P 20031112

WO 2004-US11936 W 20040416

ABSTRACT:
Methods are provided for protecting an individual from adverse long-term effects of neuroinflammation. Inflammatory blockade maintains neurogenesis capability after cranial irradn. by reducing the neg. effects of activated microglia on neural precursor cells. These findings have broad implications for a variety of diseases of cognition, involving neuroinflammation and precursor cell dysfunction.

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E2            2     PALMER THEO/IN
E3            4 --> PALMER THEO D/IN
E4            3     PALMER THEODORE D/IN
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          2167 INFLAMMATIONS
        187160 INFLAMMATION
                 (INFLAMMATION OR INFLAMMATIONS)
L2           2 ("PALMER THEO D"/IN) AND (INFLAMMATION)

=> DIS L2 1 IBIB IABS
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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L2   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:647329  CAPLUS
DOCUMENT NUMBER:          147:64553
TITLE:                    Prevention of deficits in neurogenesis with
                          antiinflammatory agents
INVENTOR(S):              Monje, Michelle L.;   ***Palmer, Theo D.***
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 49pp., Cont.-in-part of U.S.
                          Ser. No. 826,472.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2007135393	A1	20070614	US 2006-473196		20060621
US 2004254152	A1	20041216	US 2004-826472		20040416
PRIORITY APPLN. INFO.:			US 2003-463769P	P	20030417
			US 2003-519562P	P	20031112
			US 2004-826472	A2	20040416

ABSTRACT:
Methods are provided for protecting an individual from adverse long-term effects of neuroinflammation. Inflammatory blockade maintains neurogenesis capability after cranial irradn. by reducing the neg. effects of activated microglia on neural precursor cells. These findings have broad implications for a variety of diseases of cognition, involving neuroinflammation and precursor cell dysfunction.

=> DIS L2 2 IBIB IABS
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L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927009 CAPLUS
DOCUMENT NUMBER: 141:374718
TITLE: Prevention of deficits in neurogenesis with anti-inflammatory agents
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PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: PCT Int. Appl., 49 pp.
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WO 2004093802	A3	20060921		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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PRIORITY APPLN. INFO.:			US 2003-463769P	P 20030417
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REQUEST CANCELED